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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,846	02/13/2002	John N. Feder	D0079 NP	9057
23914	7590	11/03/2004	EXAMINER	
STEPHEN B. DAVIS BRISTOL-MYERS SQUIBB COMPANY PATENT DEPARTMENT P O BOX 4000 PRINCETON, NJ 08543-4000			JIANG, DONG	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,846	FEDER ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-27 and 30-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20,21,23,25,27 and 30-36 is/are rejected.
- 7) ☒ Claim(s) 22,24 and 26 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>8/19/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED OFFICE ACTION

Applicant's response filed on 06 August 2004 is acknowledged.

Currently, claims 20-27 and 30-36 are pending and under consideration.

The information disclosure statement filed on 26 August 2004 is acknowledged, and there is no PTO-1449 form accompanied with the statement.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 20, 21, 23, 25, 27 and 30-36 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by a credible, substantial, specific, or well-established utility, for the reasons of record set forth in the last Office Action mailed on 13 July 2004, at pages 2-3.

Applicants argument filed on 06 August 2004 has been fully considered, but is not deemed persuasive for reasons below.

At pages 7-8 of the response, the applicant argues that the Examiner has misconstrued the fact pattern, and the conclusions drawn are in error and not applicable to the instant invention; and that the Rappold-Hoerbrand reference does not teach that restriction sites are an essential element in the use of the HGRA4 gene in diagnosing ataxias, rather, it relied upon "Fish-analysis on metaphase spreads" to identify the ataxia association of the HGRA4 gene, which does not rely upon identification of restriction bands, rather it relies upon hybridization of a labeled probe sequence to a target sequence. This argument is not persuasive because even though Fish-analysis may be used as an alternative way to identify the breaking point of the HGRA4 gene, the analysis is based on hybridization of nucleotide sequences, which requires sequence specificity, therefore, the sequence identity of the HGRA4 gene (as a probe) is essential for the hybridization in order to pull out the exact gene for diagnosing ataxias associated with the

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HGRA4 gene. As such, the “encoding” sequence of the HGRA4 cannot be used either as a probe in hybridization, or as a normal comparison sequence for identifying the breaking point or any other abnormal changes of the gene as it encompasses sequences that have merely less than 70% sequence identity to the HGRA4 gene, and such degenerated sequences would hybridize to many other genes that are unrelated to the HGRA4 gene, and one skilled in the art would not consider such sequences as suitable probes for assays such as FisH or any other sequence based assays for the purpose of diagnosis.

At page 9 of the response, the applicant argues that the results of the Rappold-Hoerbrand experiment “shows clearly that the breakpoint of the patient resides within the genomic locus of the ataxia gene”; that as such, one skilled in the art would clearly appreciate that such a disruption in the HGRA4 genomic sequence would result in loss of the HGRA4 protein and that the loss of the HGRA4 protein is causative to the incidence of ataxia; and that one skilled in the art would readily appreciate that the analysis of HGRA4 protein expression would also represent a useful tool for the diagnosis of cerebral ataxias. This argument is not persuasive for the following reasons. First, the genomic *locus* of the ataxia gene comprises the ataxia gene, but it is not equal to the ataxia *gene*, as a genomic locus comprises many genes. Therefore, there is no evidence that the breakpoint of the patient resides within the ataxia gene, and it is unclear how the ataxia gene was affected. Further, even if the breakpoint of the patient were within the ataxia gene, the art has not established any inevitable relationship between a gene with a breakpoint and the loss of the expression of the encoded protein. Besides the possibility of loss of the protein expression, other possibilities may occur as a result of a breakpoint on a gene, such as the expression of a truncated or altered protein. Neither the Rappold-Hoerbrand reference, nor the present specification discloses any of the possibilities in this case. Therefore, in the absence of any supporting evidence regarding the HGRA4 protein expression in the patient, the relationship between the breakpoint within the genomic locus of the HGRA4 gene and the loss of HGRA4 protein expression cannot be established.

At page 10 of the response, the applicant argues that Rappold-Hoerbrand teaches that ataxia proteins can be used in the therapeutic treatment of disorders related to mutations in said genes, and cDNAs can be used for the preparation of recombinant proteins suitable for the treatment, and that both the polynucleotide and polypeptide of the HGRA4 have a specific,

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credible and well-established utility. This argument is not persuasive because Rappold-Hoerbrand does not teach any specific mutation of said ataxia gene with impaired protein expression, and how the encoded protein expression was affected (increased or decreased levels of expression, loss of the expression, or altered the form of the protein), nor any related ataxia case being treated with the taught ataxia protein. As such, the therapeutic “utility” of Rappold-Hoerbrand’s ataxia protein is neither well-established nor substantial as there is no immediately apparent or “real world” utility for the protein, and further research and experimentation are required in order to identify any practical therapeutic application for said protein. Further, until a specific and substantial utility can be attributed to the HGRA4 protein, use of the cDNAs for the preparation of the recombinant protein is not considered by the Patent Office to be a specific or substantial utility, as such use could be asserted for *any* cDNA.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20, 21, 23, 25, 27 and 30-36 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial or credible utility for the reasons of record set forth in the last Office Action mailed on 13 July 2004, at pages 4, and the reasons above, as one skilled in the art clearly would not know how to use the claimed invention.

Conclusion:

Claims 22, 24 and 26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Advisory Information:

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.


LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
10/19/04